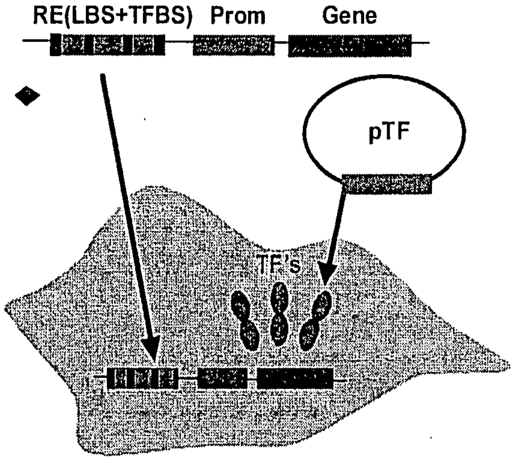


Figure 1

distal UP

nnAAA(A/T)(A/T)T(A/T)TTTTnnAAAAnnn

proximal UP

FIGURE 2A

-66 -59 UP element -38
CCGCGTCAGAAAATTATTTTAAATTTCCTCTTGTCAGGCCGGAATAACTCCCTA
AATGCGCCAC

+1 +50
CACTGACACGGAACAACGGCAAACACGCCGCCGGGTCAGCGGGGTTCTCCT

FIGURE 2B

09519297.020300

Switchable Promoter: Drug Targeting near *Cis* Element

- **Direct targeting**

MEF	C(TTAAAAATAA)C
780BP	(TTGAAAAATCAA)CGCT

- **Overlapping Targeting (test for up or down-stream)**

UL9	(ttttTGTT)CGCAC(TTtttttt)
NFκB	(tttttGGG[AtTTT)CCttttt]
LacO	(aaaaAATT)GTGAGCGCTCAC(AATTtttt)
NtBBF1	(tttACT[TTA)tttt]

Figure 3

rrnB P1 promoter UP Sequences

RLG3097	(core)	GACTGCAGTGGTACCTAGGAGG
RLG3074	(wt)	AG**AAAATTATTTTAAATTT**CCT
RLG4192		GG**AAAATTTTTTTTCAAAA**GTA
RLG4174		TG**AAATTTATTTT**GCGAAAGGG

Figure 4A

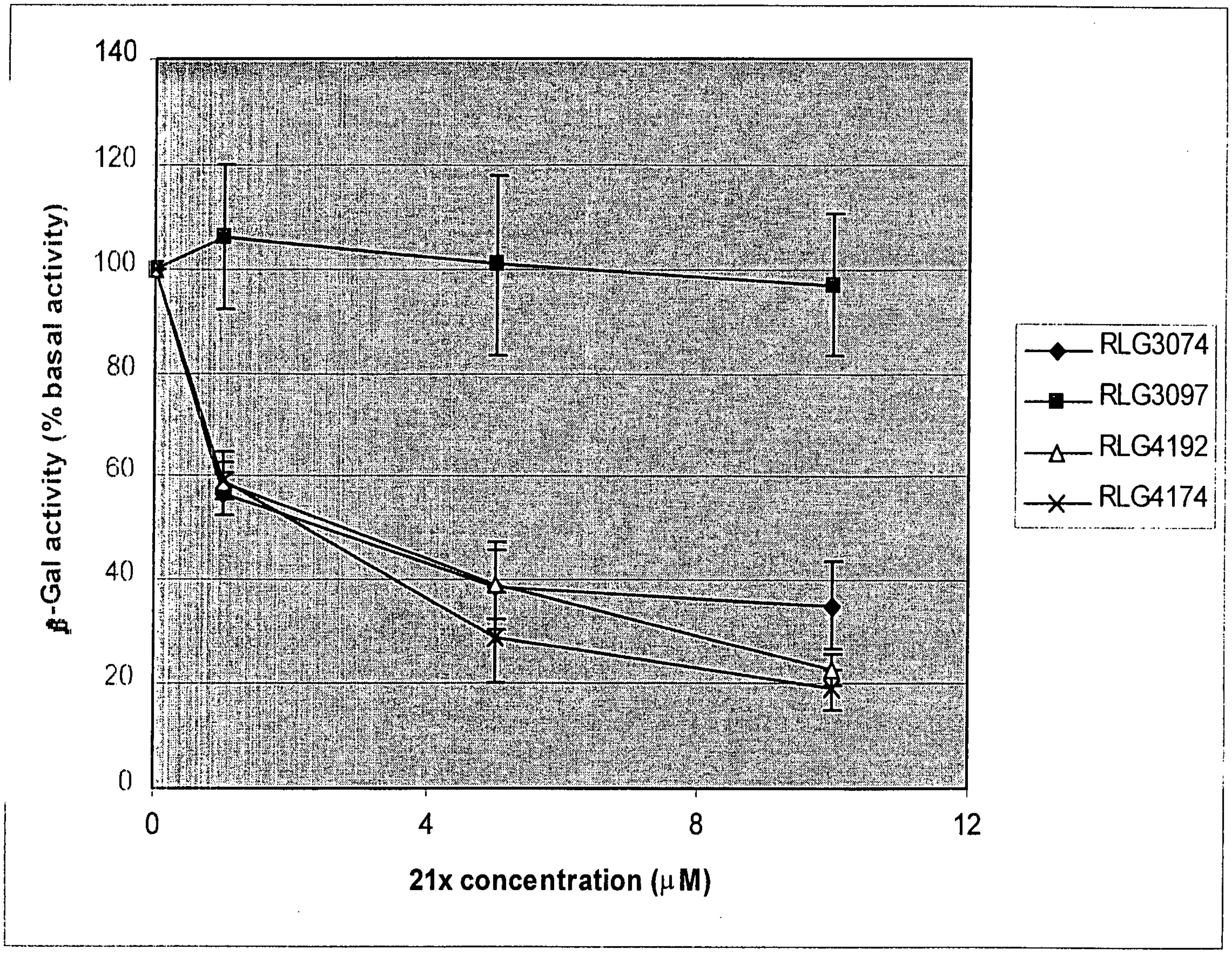

140
120
100
80
60
40
20
0
β-Gal activity (% basal activity)
0
4
8
12
21x concentration (μM)
RLG3074
RLG3097
RLG4192
RLG4174

Figure 4B

YK 202LX (52-mer) 5´ CATGGACG CCACTG AGCCGTTTT **TGTTCGCACTT** GAGGCGAGTCGATGCACC 3´
3´ GTACCTGC GGTGAC TCGGCAAAA **ACAAGCGTGAA** CTCCGCTCAGCTACGTGG 5´

YK 202RX-A (54-mer) 5´ CATGGACG CCACTG AGCCG **TGTTCGCACTT** TTTTTTGAGGCGAGTCGATGCACC 3´
YK 202RX-B (54-mer) 3´ GTACCTGC GGTGAC TCGGC **ACAAGCGTGAA** AAAAAACTCCGCTCAGCTACGTGG**B** 5´

YK 202LRX (58-mer) 5´ CATGGACG CCACTG AGCCGTTTT **TGTTCGCACTT** TTTTTTGAGGCGAGTCGATGCACC 3´
3´ GTACCTGC GGTGAC TCGGCAAAA **ACAAGCGTGAA** AAAAAACTCCGCTCAGCTACGTGG 5´

Figure 5

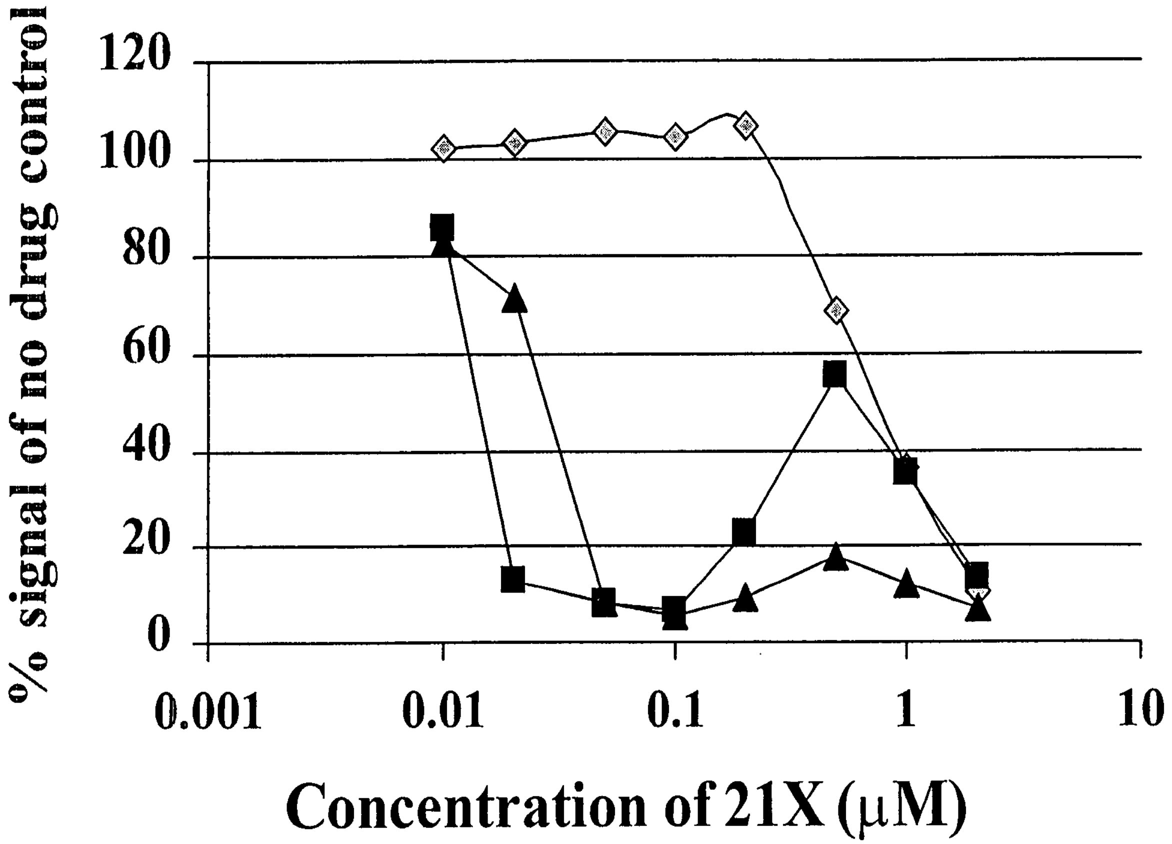

% signal of no drug control
120
100
80
60
40
20
0
0.001
0.01
0.1
1
10
Concentration of 21X (μM)

FIGURE 6

JF 101 (NFKB1) (50mer) (right side)

5′ cgac cgtgctcgag **TTAACGGGACTTTCCAAaaa** cgatcg gact ggactc 3′
3′ gctg gcacgagctc **AATTGCCCTGAAAGGTTttt** gctagc ctga cctgag 5

JF 102 (NFKB2)(60mer)(right side)

5′ cgac cgtgctcgag **TTAACGGGAtTTTCCAAaaa** cgatcg gact ggactc 3′
3′ gctg gcacgagctc **AATTGCCCTaAAAGGTTttt** gctagc ctga cctgag 5′

JF 103 (NFKB3)(60mer) (both side)

5′ cgac cgtgctcgag **aaattGGGAtTTTCCAAaaa** cgatcg gact ggactc 3′
3′ gctg gcacgagctc **tttaaCCCTaAAAGGTTttt** gctagc ctga cctgag 5′

FIGURE 7

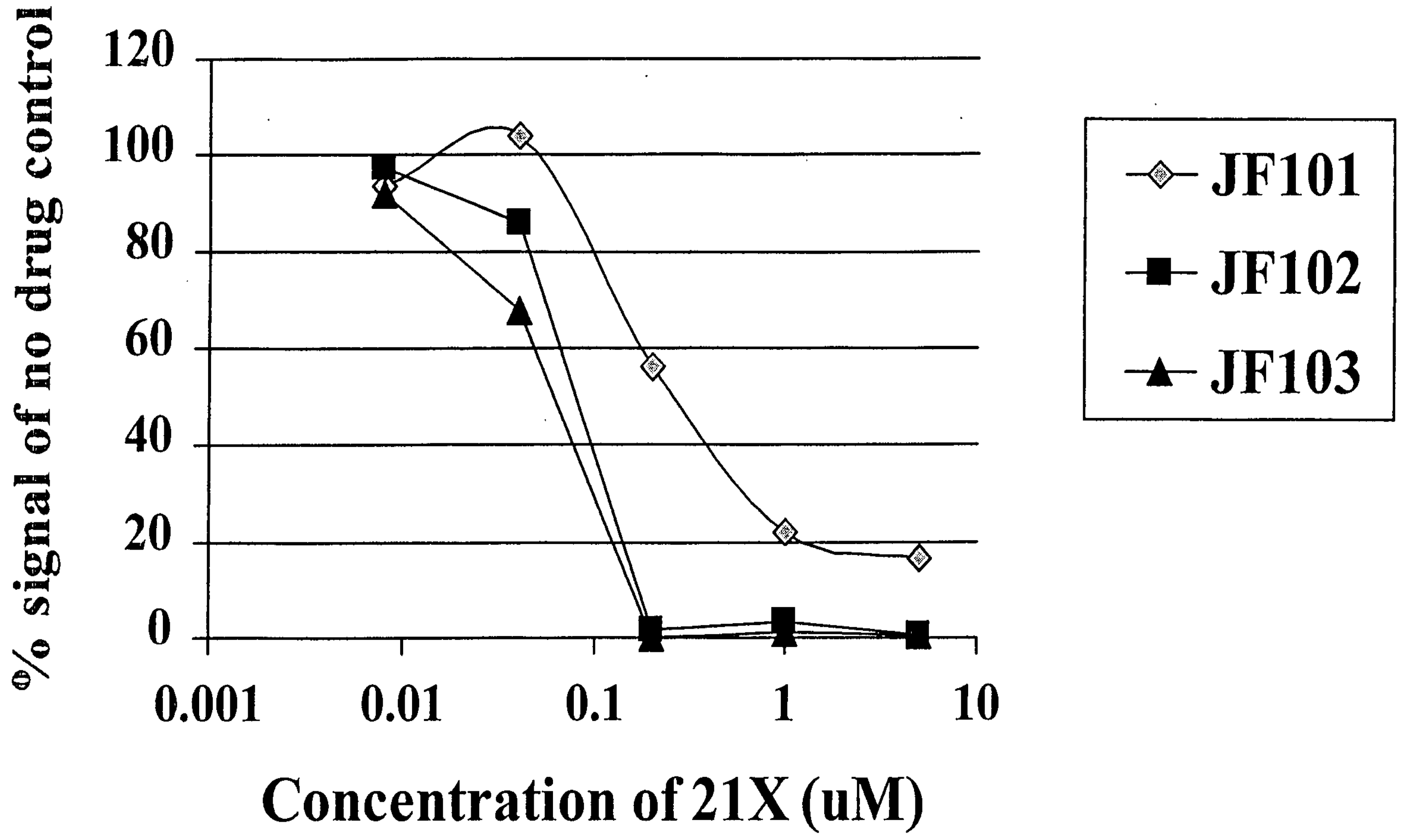

% signal of no drug control
120
100
80
60
40
20
0
0.001
0.01
0.1
1
10
Concentration of 21X (uM)
JF101
JF102
JF103

FIGURE 8A

09518297.030300

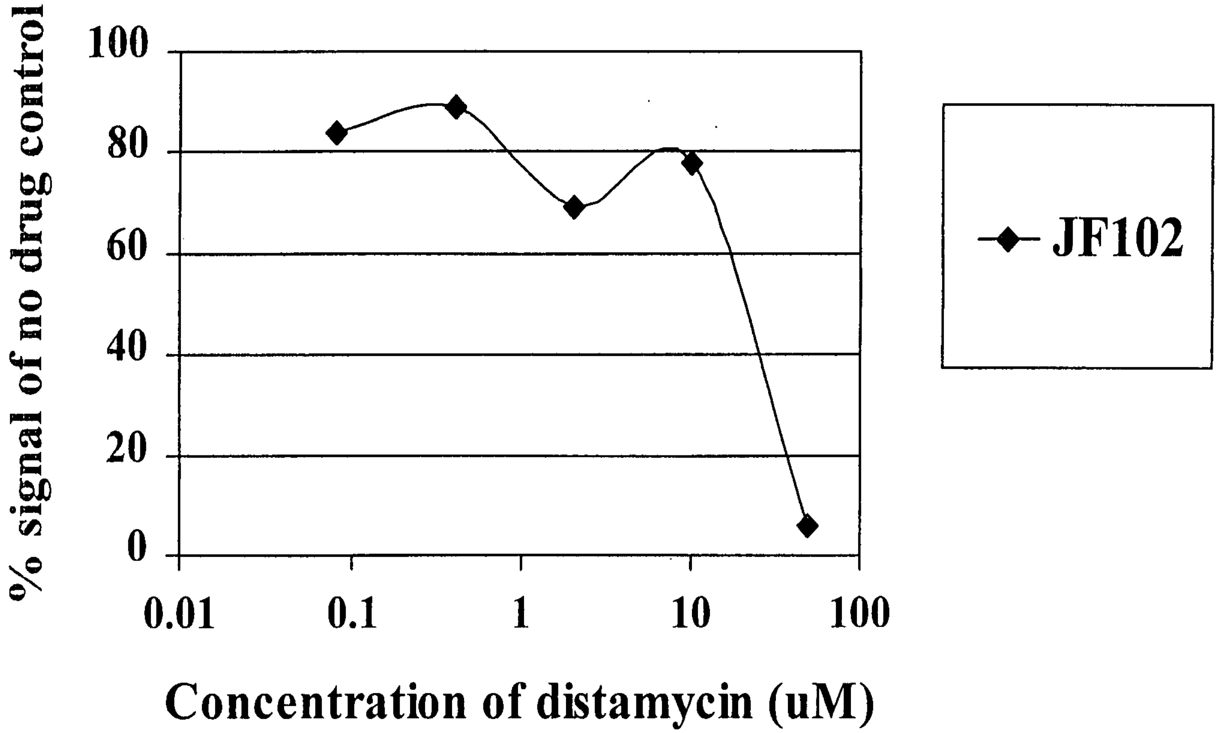


FIGURE 8B

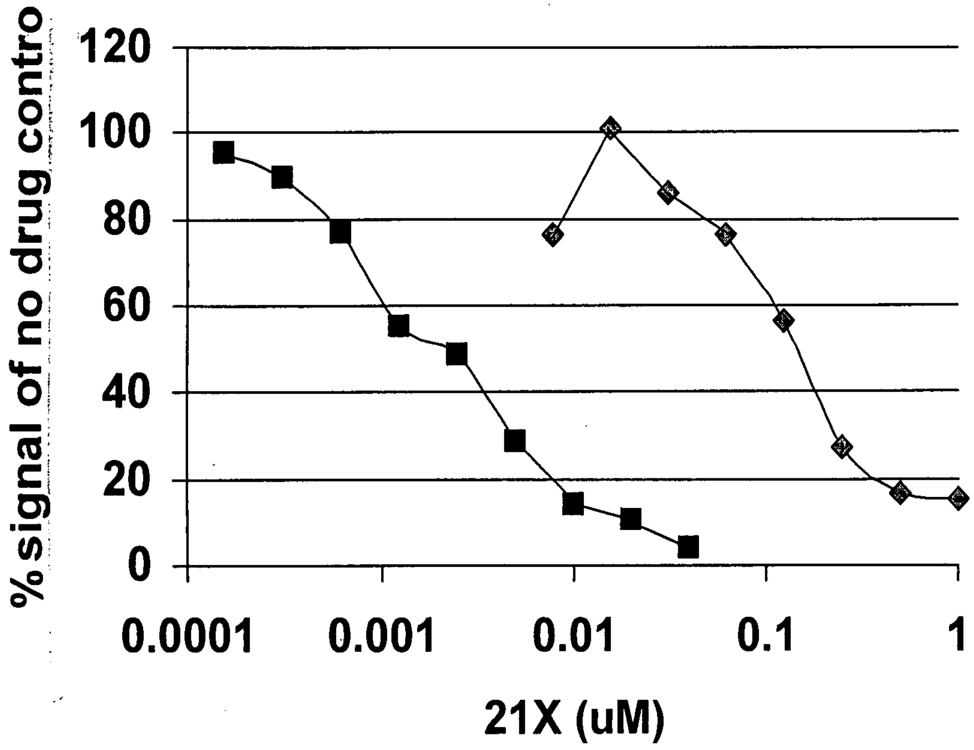
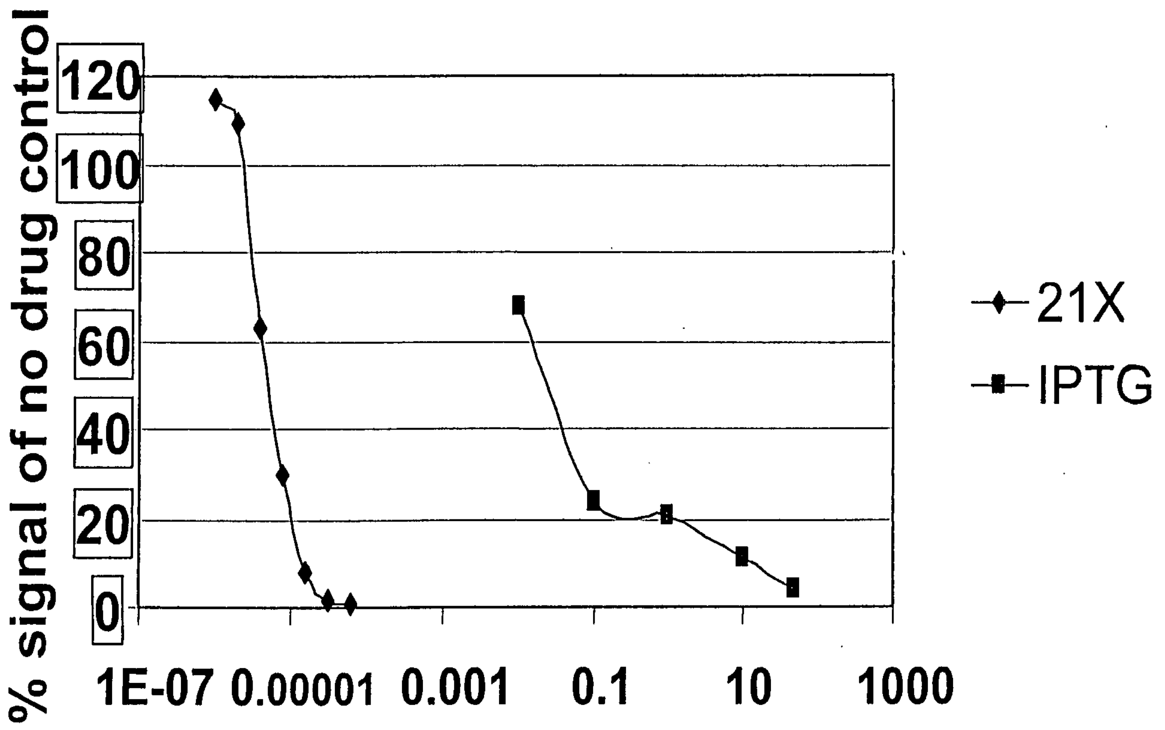

% signal of no drug contro
120
100
80
60
40
20
0
0.0001
0.001
0.01
0.1
1
21X (uM)

FIGURE 9



Concentration of drugs (mM)

FIGURE 10

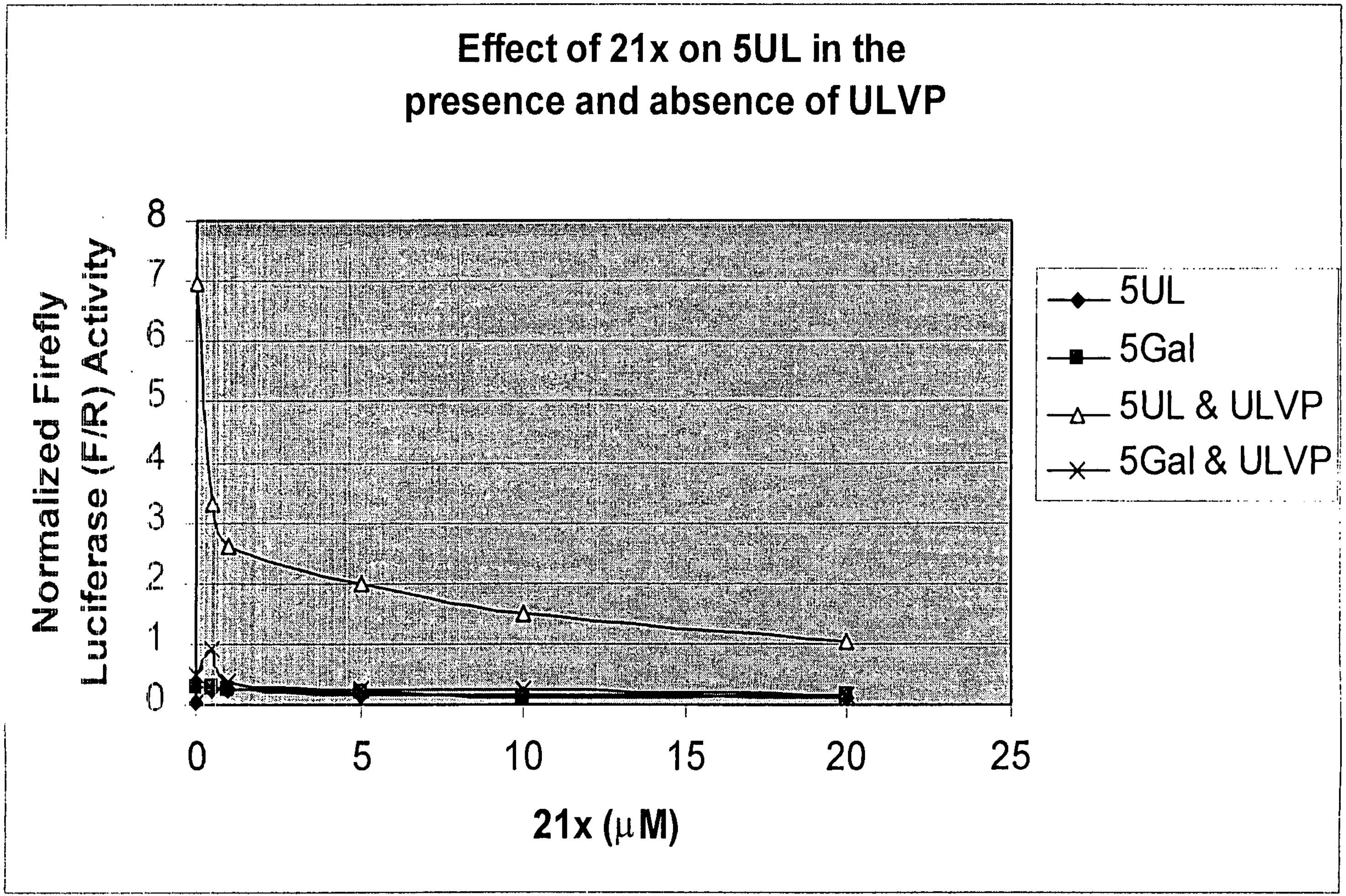

Effect of 21x on 5UL in the presence and absence of ULVP
Normalized Firefly Luciferase (F/R) Activity
8
7
6
5
4
3
2
1
0
0
5
10
15
20
25
21x (μM)
5UL
5Gal
5UL & ULVP
5Gal & ULVP

FIGURE 11

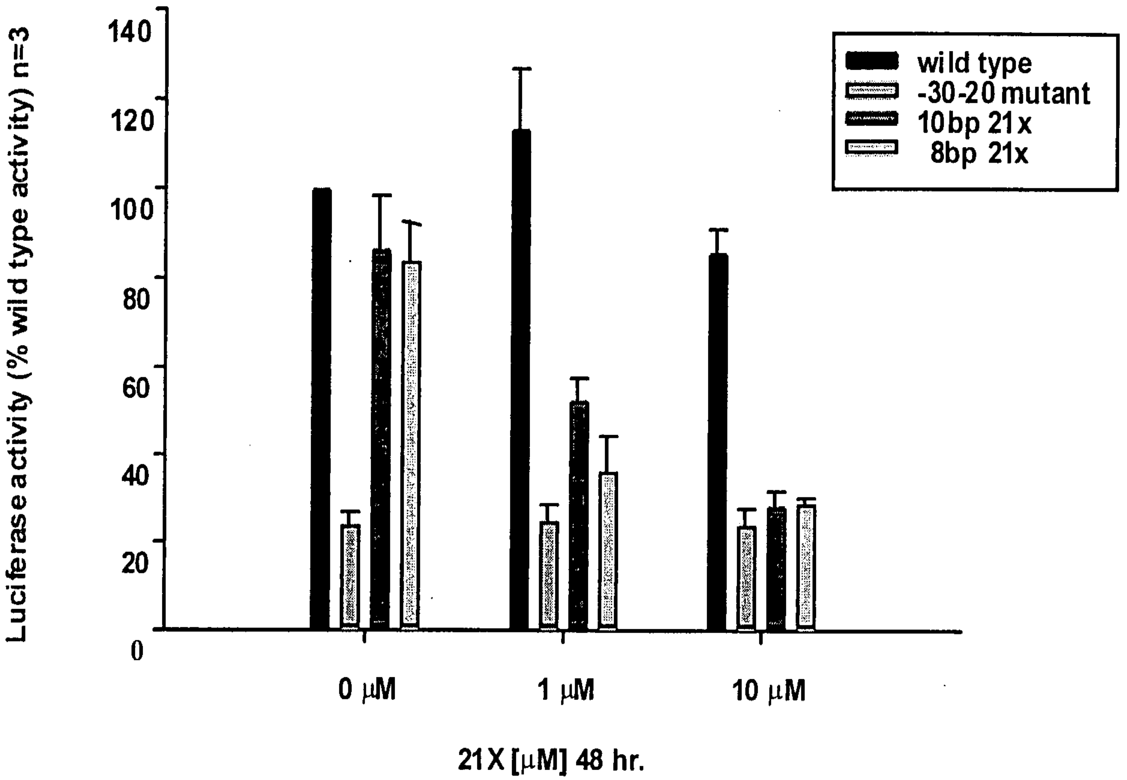

Luciferase activity (% wild type activity) n=3
140
120
100
80
60
40
20
0
0 µM
1 µM
10 µM
21X [µM] 48 hr.
wild type
-30-20 mutant
10bp 21x
8bp 21x

FIGURE 12

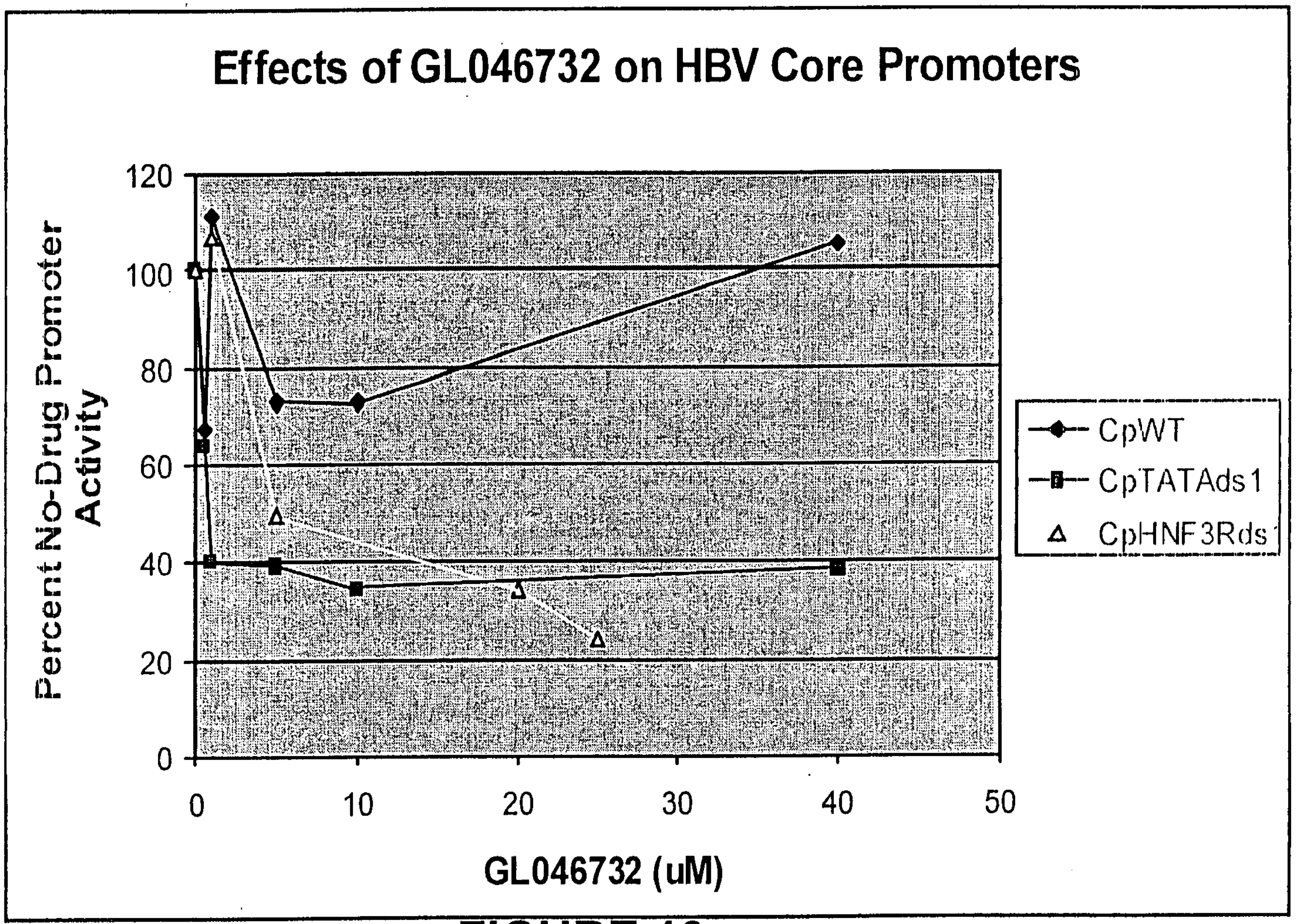

Effects of GL046732 on HBV Core Promoters
Percent No-Drug Promoter Activity
120
100
80
60
40
20
0
0
10
20
30
40
50
GL046732 (uM)
CpWT
CpTATAds1
CpHNF3Rds1

FIGURE 13

TCAATATTGGCCATTAGCCATATTATTCATTGGTTATATAGCATAAATCAATATTGGCTATTGGC
CATTGCATACGTTGTATCTATATCATAATATGTACATTTATATTGGCTCATGTCCAATATGACCG
CCATGTTGGCATTGATTATTGACTAGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCATAG
CCCATATATGGAGTTCCGCGTTACATAACTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACG
ACCCCCGCCCATTGACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCAT
TGACGTCAATGGGTGGAGTATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATAT
GCCAAGTCCGCCCCCTATTGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACA
TGACCTTACGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTG
ATGCGGTTTTGGCAGTACACCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCT
CCACCCCATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTC
GTAACAACTGCGATCGCCCGCCCCGTTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCT
ATATAAGCAGAGCTCGTTTAGTGAACCGTCAGATCACTAGAAGCTTTATTGCGGTAGTTTATCAC
AGTTAAATTGCTAACGCAGTCAGTGCTTCTGACACAACAGTCTCGAACTTAAGCTGCAGTGACTC
TCTTAAGGTAGCCTTGCAGAAGTTGGTCGTGAGGCACTGGGCAGGTAAGTATCAAGGTTACAAGA
CAGGTTTAAGGAGACCAATAGAAACTGGGCTTGTCGAGACAGAGAAGACTCTTGCGTTTCTGATA
GGCACCTATTGGTCTTACTGACATCCACTTTGCCTTTCTCTCCACAGGTGTCCACTCCCAGTTCA
ATTACAGCTCTTAAGGCTAGAGTACTTAATACGACTCACTATAGGCTAGCCAGCTTGAAGCAAGC
CTCCTGAAAGATGGAGGCGTCGCTGCCGGCCCAGGCCGCCGAGACGGAGGAGGTGGGTCTTTTCG
TCGAAAAATACCTCCGGTCCGATGTCGCGCCGGCGGAAATTGTCGCGCTCATGCGCAACCTCAAC
AGCCTGATGGGACGCACGCGGTTTATTTACCTGGCGTTGCTGGAGGCCTGTCTCCGCGTTCCCAT
GGCCACCCGCAGCAGCGCCATATTTCGGCGGATCTATGACCACTACGCCACGGGCGTCATCCCCA
CGATCAACGTCACCGGAGAGCTGGAGCTCGTGGCCCTGCCCCCCACCCTGAACGTAACCCCCGTC
TGGGAGCTGTTGTGCCTGTGCAGCACCATGGCCGCGCGCCTGCATTGGGACTCGGCGGCCGGGGG
ATCTGGGAGGACCTTCGGCCCCGATGACGTGCTGGACCTACTGACCCCCCACTACGACCGCTACA
TGCAGCTGGTGTTCGAACTGGGCCACTGTAACGTAACCGACGGACTTCTGCTCTCGGAGGAAGCC
GTCAAGCGCGTCGCCGACGCCCTAAGCGGCTGTCCCCCGCGCGGGTCCGTTAGCGAGACGGACCA
CGCGGTGGCGCTGTTCAAGATAATCTGGGGCGAACTGTTTGGCGTGCAGATGGCCAAAAGCACGC
AGACGTTTCCCGGGGCGGGGCGCGTTAAAAACCTCACCAAACAGACAATCGTGGGGTTGTTGGAC
GCCCACCACATCGACCACAGCGCCTGCCGGACCCACAGGCAGCTGTACGCCCTGCTTATGGCCCA
CAAGCGGGAGTTTGCGGGCGCGCGCTTCAAGCTACGCGTGCCCGCGTGGGGGCGCTGTTTGCGCA
CGCACTCATCCAGCGCCAACCCCAACGCTGACATCATCCTGGAGGCGGCGCTGTCGGAGCTCCCC
ACCGAGGCCTGGCCCATGATGCAGGGGGCGGTGAACTTTAGCACCCTAATGAAGCTACTGTCTTC
TATCGAACAAGCATGCCCAAAAAAGAAGAGAAAGGTAGATGAATTCCCGGGGATCTCGACGGCCC
CCCCGACCGATGTCAGCCTGGGGGACGAGCTCCACTTAGACGGCGAGGACGTGGCGATGGCGCAT
GCCGACGCGCTAGACGATTTCGATCTGGACATGTTGGGGGACGGGGATTCCCCGGGTCCGGGATC
GCCAGGGATCCGTCGACTTGACGCGTTGATATCATCTAGAGCGGCCGCAGGTACCTGAATAACTA
AGGCCGCTTCCCTTTAGTGAGGGTTAATGCTTCGAGCAGACATGATAAGATACATTGATGAGTTT
GGACAAACCACAACTAGAATGCAGTGAAAAAAATGCTTTATTTGTGAAATTTGTGATGCTATTGC
TTTATTTGTAACCATTATAAGCTGCAATAAACAAGTTAACAACAACAATTGCATTCATTTTATGT
TTCAGGTTCAGGGGGAGATGTGGGAGGTTTTTTAAAGCAAGTAAAACCTCTACAAATGTGGTAAA
ATCCGATAAGGATCGATTCCGGAGCCTGAATGGCGAATGGACGCGCCCTGTAGCGGCGCATTAAG
CGCGGCGGGTGTGGTGGTTACGCGCACGTGACCGCTACACTTGCCAGCGCCCTAGCGCCCGCTCC
TTTCGCTTTCTTCCCTTCCTTTCTCGCCACGTTCGCCGGCTTTCCCCGTCAAGCTCTAAATCGGG
GGCTCCCTTTAGGGTTCCGATTTAGTGCTTTACGGCACCTCGACCCCAAAAAACTTGATTAGGGT
GATGGTTCACGTAGTGGGCCATCGCCCTGATAGACGGTTTTTCGCCCTTTGACGTTGGAGTCCAC
GTTCTTTAATAGTGGACTCTTGTTCCAAACTGGAACAACACTCAACCCTATCTCGGTCTATTCTT
TTGATTTATAAGGGATTTTGCCGATTTCGGCCTATTGGTTAAAAAATGAGCTGATTTAACAAAAA
TTTAACGCGAATTTTAACAAAATATTAACGCTTACAATTTCGCCTGTGTACCTTCTGAGGCGGAA
AGAACCAGCTGTGGAATGTGTGTCAGTTAGGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGA
AGTATGCAAAGCATGCATCTCAATTAGTCAGCAACCAGGTGTGGAAAGTCCCCAGGCTCCCCAGC
AGGCAGAAGTATGCAAAGCATGCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGC

FIGURE 14A

CCATCCCGCCCCTAACTCCGCCCAGTTCCGCCCATTCTCCGCCCCATGGCTGACTAATTTTTTTT
ATTTATGCAGAGGCCGAGGCCGCCTCGGCCTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTT
TGGAGGCCTAGGCTTTTGCAAAAAGCTTGATTCTTCTGACACAACAGTCTCGAACTTAAGGCTAG
AGCCACCATGATTGAACAAGATGGATTGCACGCAGGTTCTCCGGCCGCTTGGGTGGAGAGGCTAT
TCGGCTATGACTGGGCACAACAGACAATCGGCTGCTCTGATGCCGCCGTGTTCCGGCTGTCAGCG
CAGGGGCGCCCGGTTCTTTTTGTCAAGACCGACCTGTCCGGTGCCCTGAATGAACTGCAGGACGA
GGCAGCGCGGCTATCGTGGCTGGCCACGACGGGCGTTCCTTGCGCAGCTGTGCTCGACGTTGTCA
CTGAAGCGGGAAGGGACTGGCTGCTATTGGGCGAAGTGCCGGGGCAGGATCTCCTGTCATCTCAC
CTTGCTCCTGCCGAGAAAGTATCCATCATGGCTGATGCAATGCGGCGGCTGCATACGCTTGATCC
GGCTACCTGCCCATTCGACCACCAAGCGAAACATCGCATCGAGCGAGCACGTACTCGGATGGAAG
CCGGTCTTGTCGATCAGGATGATCTGGACGAAGAGCATCAGGGGCTCGCGCCAGCCGAACTGTTC
GCCAGGCTCAAGGCGCGCATGCCCGACGGCGAGGATCTCGTCGTGACCCATGGCGATGCCTGCTT
GCCGAATATCATGGTGGAAAATGGCCGCTTTTCTGGATTCATCGACTGTGGCCGGCTGGGTGTGG
CGGACCGCTATCAGGACATAGCGTTGGCTACCCGTGATATTGCTGAAGAGCTTGGCGGCGAATGG
GCTGACCGCTTCCTCGTGCTTTACGGTATCGCCGCTCCCGATTCGCAGCGCATCGCCTTCTATCG
CCTTCTTGACGAGTTCTTCTGAGCGGGACTCTGGGGTTCGAAATGACCGACCAAGCGACGCCCAA
CCTGCCATCACGATGGCCGCAATAAAATATCTTTATTTTCATTACATCTGTGTGTTGGTTTTTTG
TGTGAAGATCCGCGTATGGTGCACTCTCAGTACAATCTGCTCTGATGCCGCATAGTTAAGCCAGC
CCCGACACCCGCCAACACCCGCTGACGCGCCCTGACGGGCTTGTCTGCTCCCGGCATCCGCTTAC
AGACAAGCTGTGACCGTCTCCGGGAGCTGCATGTGTCAGAGGTTTTCACCGTCATCACCGAAACG
CGCGAGACGAAAGGGCCTCGTGATACGCCTATTTTTATAGGTTAATGTCATGATAATAATGGTTT
CTTAGACGTCAGGTGGCACTTTTCGGGGAAATGTGCGCGGAACCCCTATTTGTTTATTTTTCTAA
ATACATTCAAATATGTATCCGCTCATGAGACAATAACCCTGATAAATGCTTCAATAATATTGAAA
AAGGAAGAGTATGAGTATTCAACATTTCCGTGTCGCCCTTATTCCCTTTTTTGCGGCATTTTGCC
TTCCTGTTTTTGCTCACCCAGAAACGCTGGTGAAAGTAAAAGATGCTGAAGATCAGTTGGGTGCA
CGAGTGGGTTACATCGAACTGGATCTCAACAGCGGTAAGATCCTTGAGAGTTTTCGCCCCGAAGA
ACGTTTTCCAATGATGAGCACTTTTAAAGTTCTGCTATGTGGCGCGGTATTATCCCGTATTGACG
CCGGGCAAGAGCAACTCGGTCGCCGCATACACTATTCTCAGAATGACTTGGTTGAGTACTCACCA
GTCACAGAAAAGCATCTTACGGATGGCATGACAGTAAGAGAATTATGCAGTGCTGCCATAACCAT
GAGTGATAACACTGCGGCCAACTTACTTCTGACAACGATCGGAGGACCGAAGGAGCTAACCGCTT
TTTTGCACAACATGGGGGATCATGTAACTCGCCTTGATCGTTGGGAACCGGAGCTGAATGAAGCC
ATACCAAACGACGAGCGTGACACCACGATGCCTGTAGCAATGGCAACAACGTTGCGCAAACTATT
AACTGGCGAACTACTTACTCTAGCTTCCCGGCAACAATTAATAGACTGGATGGAGGCGGATAAAG
TTGCAGGACCACTTCTGCGCTCGGCCCTTCCGGCTGGCTGGTTTATTGCTGATAAATCTGGAGCC
GGTGAGCGTGGGTCTCGCGGTATCATTGCAGCACTGGGGCCAGATGGTAAGCCCTCCCGTATCGT
AGTTATCTACACGACGGGGAGTCAGGCAACTATGGATGAACGAAATAGACAGATCGCTGAGATAG
GTGCCTCACTGATTAAGCATTGGTAACTGTCAGACCAAGTTTACTCATATATACTTTAGATTGAT
TTAAAACTTCATTTTTAATTTAAAAGGATCTAGGTGAAGATCCTTTTTGATAATCTCATGACCAA
AATCCCTTAACGTGAGTTTTCGTTCCACTGAGCGTCAGACCCCGTAGAAAAGATCAAAGGATCTT
CTTGAGATCCTTTTTTTCTGCGCGTAATCTGCTGCTTGCAAACAAAAAAACCACCGCTACCAGCG
GTGGTTTGTTTGCCGGATCAAGAGCTACCAACTCTTTTTCCGAAGGTAACTGGCTTCAGCAGAGC
GCAGATACCAAATACTGTCCTTCTAGTGTAGCCGTAGTTAGGCCACCACTTCAAGAACTCTGTAG
CACCGCCTACATACCTCGCTCTGCTAATCCTGTTACCAGTGGCTGCTGCCAGTGGCGATAAGTCG
TGTCTTACCGGGTTGGACTCAAGACGATAGTTACCGGATAAGGCGCAGCGGTCGGGCTGAACGGG
GGGTTCGTGCACACAGCCCAGCTTGGAGCGAACGACCTACACCGAACTGAGATACCTACAGCGTG
AGCTATGAGAAAGCGCCACGCTTCCCGAAGGGAGAAAGGCGGACAGGTATCCGGTAAGCGGCAGG
GTCGGAACAGGAGAGCGCACGAGGGAGCTTCCAGGGGGAAACGCCTGGTATCTTTATAGTCCTGT
CGGGTTTCGCCACCTCTGACTTGAGCGTCGATTTTTGTGATGCTCGTCAGGGGGGCGGAGCCTAT
GGAAAAACGCCAGCAACGCGGCCTTTTTACGGTTCCTGGCCTTTTGCTGGCCTTTTGCTCACATG
GCTCGACAGATCT

FIGURE 14B

```
TCAATATTGGCCATTAGCCATATTATTCATTGGTTATATAGCATAAATCAATATTGGCTATTGGC
CATTGCATACGTTGTATCTATATCATAATATGTACATTTATATTGGCTCATGTCCAATATGACCG
CCATGTTGGCATTGATTATTGACTAGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCATAG
CCCATATATGGAGTTCCGCGTTACATAACTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACG
ACCCCCGCCCATTGACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCAT
TGACGTCAATGGGTGGAGTATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATAT
GCCAAGTCCGCCCCCTATTGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACA
TGACCTTACGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTG
ATGCGGTTTTGGCAGTACACCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCT
CCACCCCATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTC
GTAACAACTGCGATCGCCCGCCCCGTTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCT
ATATAAGCAGAGCTCGTTTAGTGAACCGTCAGATCACTAGAAGCTTTATTGCGGTAGTTTATCAC
AGTTAAATTGCTAACGCAGTCAGTGCTTCTGACACAACAGTCTCGAACTTAAGCTGCAGTGACTC
TCTTAAGGTAGCCTTGCAGAAGTTGGTCGTGAGGCACTGGGCAGGTAAGTATCAAGGTTACAAGA
CAGGTTTAAGGAGACCAATAGAAACTGGGCTTGTCGAGACAGAGAAGACTCTTGCGTTTCTGATA
GGCACCTATTGGTCTTACTGACATCCACTTTGCCTTTCTCTCCACAGGTGTCCACTCCCAGTTCA
ATTACAGCTCTTAAGGCTAGAGTACTTAATACGACTCACTATAGGCTAGCCAGCTTGAAGCAAGC
CTCCTGAAAGATGGAGGCGTCGCTGCCGGCCCAGGCCGCCGAGACGGAGGAGGTGGGTCTTTTCG
TCGAAAAATACCTCCGGTCCGATGTCGCGCCGGCGGAAATTGTCGCGCTCATGCGCAACCTCAAC
AGCCTGATGGGACGCACGCGGTTTATTTACCTGGCGTTGCTGGAGGCCTGTCTCCGCGTTCCCAT
GGCCACCCGCAGCAGCGCCATATTTCGGCGGATCTATGACCACTACGCCACGGGCGTCATCCCCA
CGATCAACGTCACCGGAGAGCTGGAGCTCGTGGCCCTGCCCCCCACCCTGAACGTAACCCCCGTC
TGGGAGCTGTTGTGCCTGTGCAGCACCATGGCCGCGCGCCTGCATTGGGACTCGGCGGCCGGGGG
ATCTGGGAGGACCTTCGGCCCCGATGACGTGCTGGACCTACTGACCCCCCACTACGACCGCTACA
TGCAGCTGGTGTTCGAACTGGGCCACTGTAACGTAACCGACGGACTTCTGCTCTCGGAGGAAGCC
GTCAAGCGCGTCGCCGACGCCCTAAGCGGCTGTCCCCCGCGCGGGTCCGTTAGCGAGACGGACCA
CGCGGTGGCGCTGTTCAAGATAATCTGGGGCGAACTGTTTGGCGTGCAGATGGCCAAAAGCACGC
AGACGTTTCCCGGGGCGGGGCGCGTTAAAAACCTCACCAAACAGACAATCGTGGGGTTGTTGGAC
GCCCACCACATCGACCACAGCGCCTGCCGGACCCACAGGCAGCTGTACGCCCTGCTTATGGCCCA
CAAGCGGGAGTTTGCGGGCGCGCGCTTCAAGCTACGCGTGCCCGCGTGGGGGCGCTGTTTGCGCA
CGCACTCATCCAGCGCCAACCCCAACGCTGACATCATCCTGGAGGCGGCGCTGTCGGAGCTCCCC
ACCGAGGCCTGGCCCATGATGCAGGGGGCGGTGAACTTTAGCACCCTACCAAAAAAGAAGAGAAA
GGTAGATCGGACACTGGTGACCTTCAAGGATGTATTTGTGGACTTCACCAGGGAGGAGTGGAAGC
TGCTGGACACTGCTCAGCAGATCGTGTACAGAAATGTGATGCTGGAGAACTATAAGAACCTGGTT
TCCTTGGGTTATTGATGAGATATCATCTAGAGCGGCCGCAGGTACCTGAATAACTAAGGCCGCTT
CCCTTTAGTGAGGGTTAATGCTTCGAGCAGACATGATAAGATACATTGATGAGTTTGGACAAACC
ACAACTAGAATGCAGTGAAAAAAATGCTTTATTTGTGAAATTTGTGATGCTATTGCTTTATTTGT
AACCATTATAAGCTGCAATAAACAAGTTAACAACAACAATTGCATTCATTTTATGTTTCAGGTTC
AGGGGGAGATGTGGGAGGTTTTTTAAAGCAAGTAAAACCTCTACAAATGTGGTAAAATCCGATAA
GGATCGATTCCGGAGCCTGAATGGCGAATGGACGCGCCCTGTAGCGGCGCATTAAGCGCGGCGGG
TGTGGTGGTTACGCGCACGTGACCGCTACACTTGCCAGCGCCCTAGCGCCCGCTCCTTTCGCTTT
CTTCCCTTCCTTTCTCGCCACGTTCGCCGGCTTTCCCCGTCAAGCTCTAAATCGGGGGCTCCCTT
TAGGGTTCCGATTTAGTGCTTTACGGCACCTCGACCCCAAAAAACTTGATTAGGGTGATGGTTCA
CGTAGTGGGCCATCGCCCTGATAGACGGTTTTTCGCCCTTTGACGTTGGAGTCCACGTTCTTTAA
TAGTGGACTCTTGTTCCAAACTGGAACAACACTCAACCCTATCTCGGTCTATTCTTTTGATTTAT
AAGGGATTTTGCCGATTTCGGCCTATTGGTTAAAAAATGAGCTGATTTAACAAAAATTTAACGCG
AATTTTAACAAAATATTAACGCTTACAATTTCGCCTGTGTACCTTCTGAGGCGGAAAGAACCAGC
TGTGGAATGTGTGTCAGTTAGGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAGTATGCAA
AGCATGCATCTCAATTAGTCAGCAACCAGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAG
TATGCAAAGCATGCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGCCCATCCCGC
```

FIGURE 15A

```
CCCTAACTCCGCCCAGTTCCGCCCATTCTCCGCCCCATGGCTGACTAATTTTTTTTATTTATGCA
GAGGCCGAGGCCGCCTCGGCCTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCT
AGGCTTTTGCAAAAAGCTTGATTCTTCTGACACAACAGTCTCGAACTTAAGGCTAGAGCCACCAT
GATTGAACAAGATGGATTGCACGCAGGTTCTCCGGCCGCTTGGGTGGAGAGGCTATTCGGCTATG
ACTGGGCACAACAGACAATCGGCTGCTCTGATGCCGCCGTGTTCCGGCTGTCAGCGCAGGGGCGC
CCGGTTCTTTTTGTCAAGACCGACCTGTCCGGTGCCCTGAATGAACTGCAGGACGAGGCAGCGCG
GCTATCGTGGCTGGCCACGACGGGCGTTCCTTGCGCAGCTGTGCTCGACGTTGTCACTGAAGCGG
GAAGGGACTGGCTGCTATTGGGCGAAGTGCCGGGGCAGGATCTCCTGTCATCTCACCTTGCTCCT
GCCGAGAAAGTATCCATCATGGCTGATGCAATGCGGCGGCTGCATACGCTTGATCCGGCTACCTG
CCCATTCGACCACCAAGCGAAACATCGCATCGAGCGAGCACGTACTCGGATGGAAGCCGGTCTTG
TCGATCAGGATGATCTGGACGAAGAGCATCAGGGGCTCGCGCCAGCCGAACTGTTCGCCAGGCTC
AAGGCGCGCATGCCCGACGGCGAGGATCTCGTCGTGACCCATGGCGATGCCTGCTTGCCGAATAT
CATGGTGGAAAATGGCCGCTTTTCTGGATTCATCGACTGTGGCCGGCTGGGTGTGGCGGACCGCT
ATCAGGACATAGCGTTGGCTACCCGTGATATTGCTGAAGAGCTTGGCGGCGAATGGGCTGACCGC
TTCCTCGTGCTTTACGGTATCGCCGCTCCCGATTCGCAGCGCATCGCCTTCTATCGCCTTCTTGA
CGAGTTCTTCTGAGCGGGACTCTGGGGTTCGAAATGACCGACCAAGCGACGCCCAACCTGCCATC
ACGATGGCCGCAATAAAATATCTTTATTTTCATTACATCTGTGTGTTGGTTTTTTGTGTGAAGAT
CCGCGTATGGTGCACTCTCAGTACAATCTGCTCTGATGCCGCATAGTTAAGCCAGCCCCGACACC
CGCCAACACCCGCTGACGCGCCCTGACGGGCTTGTCTGCTCCCGGCATCCGCTTACAGACAAGCT
GTGACCGTCTCCGGGAGCTGCATGTGTCAGAGGTTTTCACCGTCATCACCGAAACGCGCGAGACG
AAAGGGCCTCGTGATACGCCTATTTTTATAGGTTAATGTCATGATAATAATGGTTTCTTAGACGT
CAGGTGGCACTTTTCGGGGAAATGTGCGCGGAACCCCTATTTGTTTATTTTTCTAAATACATTCA
AATATGTATCCGCTCATGAGACAATAACCCTGATAAATGCTTCAATAATATTGAAAAAGGAAGAG
TATGAGTATTCAACATTTCCGTGTCGCCCTTATTCCCTTTTTTGCGGCATTTTGCCTTCCTGTTT
TTGCTCACCCAGAAACGCTGGTGAAAGTAAAAGATGCTGAAGATCAGTTGGGTGCACGAGTGGGT
TACATCGAACTGGATCTCAACAGCGGTAAGATCCTTGAGAGTTTTCGCCCCGAAGAACGTTTTCC
AATGATGAGCACTTTTAAAGTTCTGCTATGTGGCGCGGTATTATCCCGTATTGACGCCGGGCAAG
AGCAACTCGGTCGCCGCATACACTATTCTCAGAATGACTTGGTTGAGTACTCACCAGTCACAGAA
AAGCATCTTACGGATGGCATGACAGTAAGAGAATTATGCAGTGCTGCCATAACCATGAGTGATAA
CACTGCGGCCAACTTACTTCTGACAACGATCGGAGGACCGAAGGAGCTAACCGCTTTTTTGCACA
ACATGGGGGATCATGTAACTCGCCTTGATCGTTGGGAACCGGAGCTGAATGAAGCCATACCAAAC
GACGAGCGTGACACCACGATGCCTGTAGCAATGGCAACAACGTTGCGCAAACTATTAACTGGCGA
ACTACTTACTCTAGCTTCCCGGCAACAATTAATAGACTGGATGGAGGCGGATAAAGTTGCAGGAC
CACTTCTGCGCTCGGCCCTTCCGGCTGGCTGGTTTATTGCTGATAAATCTGGAGCCGGTGAGCGT
GGGTCTCGCGGTATCATTGCAGCACTGGGGCCAGATGGTAAGCCCTCCCGTATCGTAGTTATCTA
CACGACGGGGAGTCAGGCAACTATGGATGAACGAAATAGACAGATCGCTGAGATAGGTGCCTCAC
TGATTAAGCATTGGTAACTGTCAGACCAAGTTTACTCATATATACTTTAGATTGATTTAAAACTT
CATTTTTAATTTAAAAGGATCTAGGTGAAGATCCTTTTTGATAATCTCATGACCAAAATCCCTTA
ACGTGAGTTTTCGTTCCACTGAGCGTCAGACCCCGTAGAAAAGATCAAAGGATCTTCTTGAGATC
CTTTTTTTCTGCGCGTAATCTGCTGCTTGCAAACAAAAAAACCACCGCTACCAGCGGTGGTTTGT
TTGCCGGATCAAGAGCTACCAACTCTTTTTCCGAAGGTAACTGGCTTCAGCAGAGCGCAGATACC
AAATACTGTCCTTCTAGTGTAGCCGTAGTTAGGCCACCACTTCAAGAACTCTGTAGCACCGCCTA
CATACCTCGCTCTGCTAATCCTGTTACCAGTGGCTGCTGCCAGTGGCGATAAGTCGTGTCTTACC
GGGTTGGACTCAAGACGATAGTTACCGGATAAGGCGCAGCGGTCGGGCTGAACGGGGGGTTCGTG
CACACAGCCCAGCTTGGAGCGAACGACCTACACCGAACTGAGATACCTACAGCGTGAGCTATGAG
AAAGCGCCACGCTTCCCGAAGGGAGAAAGGCGGACAGGTATCCGGTAAGCGGCAGGGTCGGAACA
GGAGAGCGCACGAGGGAGCTTCCAGGGGGAAACGCCTGGTATCTTTATAGTCCTGTCGGGTTTCG
CCACCTCTGACTTGAGCGTCGATTTTTGTGATGCTCGTCAGGGGGGCGGAGCCTATGGAAAAACG
CCAGCAACGCGGCCTTTTTACGGTTCCTGGCCTTTTGCTGGCCTTTTGCTCACATGGCTCGACAG
ATCT
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FIGURE 15B